

Amendment and Response

Applicant: Winthrop D. Childers et al.

Serial No.: 10/808,803

Filed: March 25, 2004

Docket No.: 200314139-1

Title: METHOD OF SORTING CELLS IN SERIES

IN THE CLAIMS

Please cancel claims 9-10, 14, 18-19, 21, 23-24, and 26-27.

Please add claims 28-29.

Please amend claims 1, 4-6, 11-12, 15-17, 20, 22, and 25 as follows:

1. (Currently Amended) A method of sorting cells comprising:

providing a fluid flow path for moving cells ~~movement~~ through a series of cell sorters in a first direction with an output of a preceding cell sorter of the series communicating with an input of a successive cell sorter of the series;

separating, within each cell sorter, a first portion of the cells away from a second portion of the cells and toward the output of a respective cell sorter by applying a first temporally varying non-uniform electric field via a first electrode array to cause movement of the first portion of the cells in a second direction across the fluid flow path, the second direction having a component generally transverse to the first direction, ~~into the output of a respective cell sorter;~~

wherein separating the first portion of the cells from the second portion of the cells further includes ~~at least one of:~~

~~applying the first non-uniform electric field as a temporally varying non-uniform electric field at a different frequency in at least two cell sorters of the series;~~

interposing the fluid flow path in each cell sorter between the first electrode array and a second electrode array that is vertically disposed relative to the first electrode array, and applying a second temporally varying non-uniform electric field from the second electrode array to ~~cause~~maintain transport of the first portion and the second portion of cells along the fluid flow path in the first direction during movement of the first portion of cells across the fluid flow path in the second direction; ~~and~~

~~applying the first non-uniform electric field as a plurality of discrete non-uniform electric fields successively applied at different positions along the fluid flow path.~~

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2. (Original) The method of claim 1 wherein the first portion of the cells are target cells to be collected and the second portion of the cells are non-target cells to be discarded.

3. (Original) The method of claim 1 wherein the second portion of the cells are target cells to be collected and the first portion of the cells are non-target cells to be discarded.

4. (Currently Amended) The method of claim 1, further comprising wherein applying the first non-uniform electric field as a first temporally varying non-uniform electric field in at least two cell sorters of the series via~~comprises:~~

applying a first frequency at a first cell sorter of the at least two cell sorters of the series, wherein the first frequency corresponds to a frequency at which the first portion of the cells and a third portion of the cells respond to the electric field with movement in the second direction and at which the second portion of the cells responds substantially less to the electric field with movement in the second direction; and

applying a second frequency at a second cell sorter of the at least two cell sorters of the series, wherein the second frequency corresponds to a frequency at which the first portion of the cells respond to the electric field with movement in the second direction and at which the third portion of the cells responds substantially less to the electric field with movement in the second direction.

5. (Currently Amended) The method of claim 1, further comprising wherein applying the first non-uniform electric field as a first temporally varying non-uniform electric field in at least two cell sorters of the series via~~comprises:~~

applying the temporally varying non-uniform electric field at a different frequency in three or more cells sorters, wherein the different frequency in each cell sorter corresponds to a frequency at which the first portion of cells responds to the electric field with movement in the second direction and at which at least one of a plurality of portions of the cells, including the second portion of the cells, responds substantially less to the electric field with movement in the second direction.

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6. (Currently Amended) The method of claim 1 wherein interposing the fluid flow path between the first electrode array and the second electrode array comprises:

arranging the first electrode array as a plurality of electrode elements generally parallel to each other in a spaced relationship with each electrode element generally parallel to a longitudinal axis of the fluid flow path; and

arranging the second electrode array as a plurality of electrode elements generally parallel to each other in a spaced relationship with each electrode element generally perpendicular to the longitudinal axis of the fluid flow path; and

~~wherein interposing the fluid flow path between the first electrode array and the second electrode array comprises vertically disposing the first electrode array relative to the second electrode array with the fluid flow path disposed between the first electrode array and the second electrode array.~~

7. (Original) The method of claim 1 further comprising:

applying the first temporally varying non-uniform electric field alternately with applying the second temporally varying non-uniform electric field.

8. (Original) The method of claim 1 wherein the first temporally varying non-uniform electric field has a first operating frequency and the second temporally varying non-uniform electric field has a second operating frequency different than the first operating frequency.

9-10. (Canceled)

11. (Currently Amended) A cell sorter system for a biodevice comprising:

a plurality of cell sorters arranged in series including a first cell sorter and a second sorter, wherein with each respective cell sorter includesing:

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a fluid flow ~~mechanism~~path configured to maintain a fluid flow for the
~~passage~~of cells in a first direction from an input to a first flow outlet and to a
second flow outlet; and

an electrode array configured to apply a temporally varying non-uniform
electric field to the cells to move at least one portion of the cells in a second direction
having a component generally transverse to the first direction, ~~to cause separation of~~
~~a first portion of the cells into a first port and a second portion of the cells into a~~
~~second port~~

wherein ~~the electrode arrays within at least two cell sorters in the series are configured~~
~~for operation at different frequencies and the first flow outlet of port of a preceding the first~~
~~cell sorter in the series is in communication with the~~ an input of the second ~~a subsequent cell~~
~~sorter in the series,~~

wherein the electrode array of the first cell sorter applies the temporally varying non-
uniform electric field at a first frequency to cause movement of a first portion and a third
portion of the cells in the second direction away from a second portion of cells until only the
first portion and the third portion of cells are positioned to enter the first flow outlet of the
first cell sorter while the fluid flow of the respective first and third portions of cells is
maintained in the first direction for passage into the first flow outlet of the first cell sorter,
and

further wherein the electrode array of the second cell sorter applies the temporally
varying non-uniform electric field at a second frequency to cause movement of the first
portion of the cells in the second direction away from the third portion of cells until only the
first portion of cells is positioned to enter the first flow outlet of the second cell sorter ~~port~~
while the fluid flow of the first portion of the cells is maintained in the first direction for
passage into the first flow outlet of the second cell sorter.

12. (Currently Amended) The cell sorter system of claim 11 wherein ~~the different~~
~~frequencies for the electrode arrays of the at least two cell sorters comprise a first frequency~~
~~and a second frequency with the first portion of the cells in each of the at least two cell~~
~~sorters responding to the electric field with movement in the second direction and the second~~
~~portion of the cells in each of the~~ first and second cell sorters responding ~~ing~~ substantially less to

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the temporally varying non-uniform electric field than the first portion or the third portion of the cells.

13. (Original) The cell sorter system of claim 11 wherein the first portion of the cells is a target group of cells and the second portion of the cells is a non-target group of cells.

14. (Canceled)

15. (Currently Amended) The cell sorter system of claim 11 further comprising:
a signal generator in communication with the electrode array of each cell sorter and configured to apply thea first frequency to the electrode array of thea first cell sorter and to apply the-a second frequency to the electrode array of thea second cell sorter~~of the plurality of cell sorters, and a third frequency to a third cell sorter of the plurality of cell sorters.~~

16. (Currently Amended) The cell sorter system of claim 11 further comprising:
a cell diverter disposed within the fluid flow path of each respective cell sorter and configured for separating the first and third portions of the cells into the first ~~port~~ flow outlet and the second portion of the cells into the second flow outlet~~port~~.

17. (Currently Amended) A cell sorter system for a biodevice comprising:
a plurality of cell sorters arranged in series with ~~at least one~~ each cell sorter of the series including:

a fluid flow path configured for directing a flow of cells in a first direction;

an electrode arrangement including a first electrode array and a second electrode array with the first electrode array configured to apply a first temporally varying non-uniform electric field for causing movement of a field-responsive portion of the cells in a second direction having a component generally transverse to the first direction and the second electrode array configured to apply a second temporally varying non-uniform electric field for causing transport of the cells along the fluid flow path in the first direction, wherein the first electrode array and the second electrode array are vertically disposed relative to one another on opposite sides of the fluid flow path with the fluid flow path interposed between

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the respective first and second electrode arrays; and

a cell diverter disposed within the fluid flow pathway to encourage separation of the field-responsive portion of the cells from a non-responsive portion of the cells.

18-19. (Canceled)

20. (Currently Amended) The cell sorter system of claim ~~22~~17 wherein ~~each of the first electrode array and the second electrode array comprise:~~

~~a plurality of electrode elements arranged generally parallel to each other with a long axis of each electrode element generally perpendicular to movement of the cells caused by the first and second electrode arrays, and wherein the array of plurality of electrode elements of each of the first and second electrode structure arrays are~~is arranged with selective electrode elements connected together to define independently drivable sets of electrode elements.

21. (Canceled)

22. (Currently Amended) A cell sorter system for a biodevice comprising:

a plurality of cell sorters arranged in series with each cell sorter including:

a fluid flow pathway including a first end; and a second end, and configured for directing a flow of cells in a first direction from the first end to the second end, the cells including a first portion and a second portion;

an electrode arrangement configured for causing movement of ~~only the a~~ first portion of the cells in a second direction generally transverse to the first direction and away from the second portion of the cells by successive discrete movements of the first portion of the cells in the second direction, wherein the electrode arrangement includes:

a first electrode structure including an array of generally parallel, spaced apart electrode elements arranged in series along a first side of the fluid flow pathway, wherein a longitudinal axis of each electrode element extends across the fluid flow pathway perpendicular to the first direction, and further wherein a length of the

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respective electrode elements increases successively from the first end to the second end of the fluid flow pathway; and

a second electrode structure disposed on a second side of the fluid flow pathway and spaced from the first electrode structure,

wherein the fluid flow pathway is interposed between the first electrode structure and the second electrode structure, and wherein the electrode structures are configured to apply a plurality of separate non-uniform electric fields successively one at a time from the first end to the second end of the fluid flow pathway with each separate non-uniform electric field being applied across the fluid flow pathway from each one of the respective electrode elements of the first electrode structure to a corresponding one of the respective electrode elements of the second electrode structure; and

a cell diverter disposed within, and adjacent to the second end of, the fluid flow pathway to encourage further separation of the first portion of the cells, that have been moved in the second direction, away from the second portion of the cells.

23-24. (Canceled)

25. (Currently Amended) The cell sorter system of claim ~~23~~ 22 wherein each electrode element has a generally sharpened end from which each of the respective ~~the~~ electric fields is applied.

26-27. (Canceled)

28. (New) A cell sorter system for a biodevice comprising:
a plurality of cell sorters arranged in series with at least one cell sorter of the series including:
a fluid flow path configured for directing a flow of cells in a first direction;
an electrode arrangement including a first electrode array and a second electrode array with the first electrode array configured to apply a first temporally varying non-uniform electric field for causing movement of a field-responsive portion of the cells in a second

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direction having a component generally transverse to the first direction and the second electrode array configured to apply a second temporally varying non-uniform electric field for causing transport of the cells along the fluid flow path in the first direction, wherein the second electrode array extends from a main portion of the fluid flow path into and through a first port of the fluid flow path, and into and through a second port of the fluid flow path; and

a cell diverter disposed within the fluid flow pathway to encourage separation of the field-responsive portion of the cells from a non-responsive portion of the cells.

29. (New) A cell sorter system for a biodevice comprising:

a plurality of cell sorters arranged in series with each cell sorter including:

a fluid flow pathway configured for directing a flow of cells in a first direction;

an electrode arrangement configured for causing movement of a first portion of the cells in a second direction generally transverse to the first direction by successive discrete movements of the first portion of the cells in the second direction, the electrode arrangement including:

a first electrode structure including an array of spaced electrode elements arranged in series along a first side of the fluid flow path; and

a second electrode structure disposed on a second side of the fluid flow path and spaced from the first electrode structure,

wherein the first and second electrode structures are configured to apply a plurality of non-uniform electric fields with each non-uniform electric field applied between a separate electrode element of the first electrode structure and the second electrode structure,

further wherein each respective electrode element has a generally sharpened end from which the electric field is applied; and

a cell diverter disposed within the fluid flow pathway to encourage separation of the first portion of the cells from a second portion of the cells.